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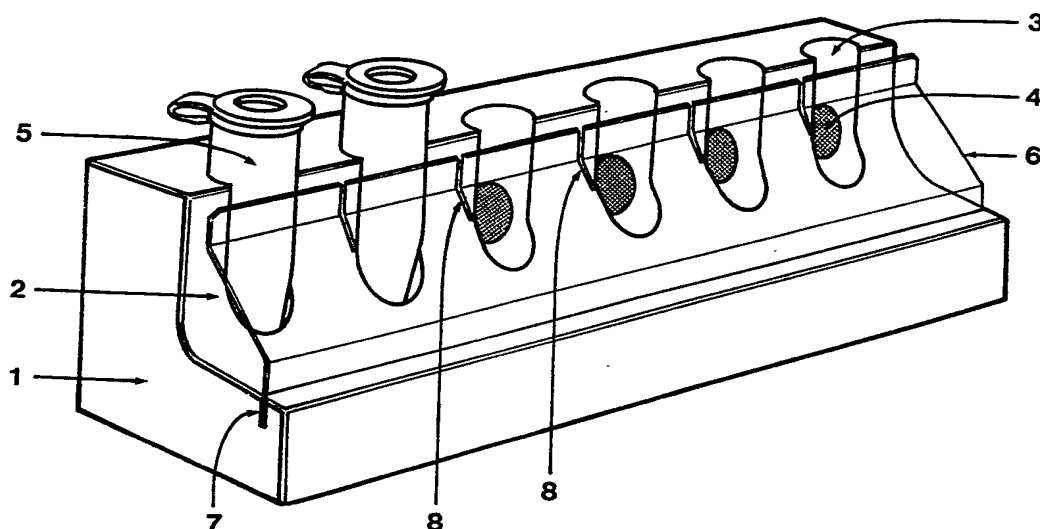
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[NO/NO]; Munkerudåsen 40B, N-1165 Oslo 11 (NO).(74) Agent: BERG, K., O.; Oslo Patentkontor A/S, P.O. Box
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(54) Title: SEPARATOR DEVICE FOR MAGNETIC PARTICLES



(57) Abstract

Separation device for separating magnetizable particles provided with a coating for selective affinity for one or more compounds to be removed from a liquid in which the particles are suspended, consisting of a rack (1) for tubes (5), preferably "Eppendorf" tubes and which rack is provided with at least one magnet that will affect the magnetizable particles when a tube is inserted in the rack, where the rack for receiving a number of tubes (5) is provided with a number of apertures (3), which tubes intersect the fields of forces from the magnet (4).

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SEPARATOR DEVICE FOR MAGNETIC PARTICLES.

Present invention relates a separation device, more specific
a separation device where a magnetic or magnetizable
carrier material in the form of particles are being separated
5 from a liquid composition.

In the fields of chemistry, biochemistry and genmanipulation
such a technique for separation has a wide application. The
magnetic carrier in the form of magnetic particles will in
10 such an application be coated with a reactive coating that
can have affinity to certain proteins, cells, vira etc. that
when a suspension containing the magnetic carrier particles
the component for which the particles have affinity, be
bound to the particles whereafter these can be separated
15 form the suspension by means of one ore more magnets. In Us
patent application 064.040 filed june 12, 1987 titled
"Magnetic Particles Concentrator", it is described a device
suited for such separation. This device consists of a rack
where a series of magnets are positioned in a row in
20 vertical direction and which device is designed to receive
a vial which is fixed by means of a springloaded clip. When
the vial is fixed in the rack, the magnets will be in
immediate proximity to the vial and the magnetic filed can
affect the suspended magnetic particles that are dispersed
25 in an solution in the vial. The particles will be collected
and concentrated along the wall of the vial and can be
collected i the bottom of the vial if it is gently pulled up
of the rack, if this is wanted.

30 The liquid in the vial, after concentration of the particles
along the wall, can be decanted from or aspired while the
particles still are fixed to the wall and new liquid can be
delivered to wash the particles etc.

35 The disadvantage with the known rack or separation device is
that it is relatively large and not suitable for utilization
of the so-called "Eppendorf-tubes" or micro test tubes which

are widely used in the field of macromolecular research. It is also difficult with this known device to arrange more vials in one rack due to the manually operated fix/clip-device for fixation of the vials with content.

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It is therefore a need for a simple separation device which can contain more vials or "Eppendorf-tubes" and where fixation of one tube by means of manually operated fixing-device can be avoided.

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The present separation device eliminates these disadvantages and make it possible to fixate numerous vials or "Eppendorf" tubes for simultaneous treatment. Preferably the centre distance between each tube is such that the liquid can be drawn off by means of an automatic standard pipette.

15

This is accomplished with the separation device according to present invention by that it contains a block with numerous semi circular apertures that can receive a "Eppendorf" tube, when a section of the aperture has a design that is corresponding to the outer contour of the "Eppendorf" tube. In the block it is arranged strong permanent and electro-magnets that will be adjacent to the sidewall in a "Eppendorf" tube when this is placed in one of the apertures.

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To avoid that the tubes can fall out of the apertures when the separation device is shaken or turned, the tubes will be fixated by means of an elastic plate arranged in front of the tubes that apply an elastic force and fixate the tubes in the rack.

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The invention will be further explained with reference to the accompanying drawing which shows a preferred embodiment of the invention. In the drawing reference number 1 designate a block of a non-magnetic material which material preferably is easy to keep clean and easy machineable. An example of such a material is "Teflon".

35

The block 1 is provided with an aperture 2 which extends in the longitudinal direction. In this aperture 2 is provided a number of vertical extending apertures 3 to receive "Eppendorf" tubes 5. Adjacent each aperture 3 is provided at least one magnet 4 that will adjacent the sidewall of the "Eppendorf" tube 5 when this is inserted in an aperture 3. For fixation of a tube 5, the block 1 is provided with a longitudinal slot in which it is inserted an fixed a suitable designed plate 6 which upper edge will elasticly be resting against a tube 5 inserted in the aperture 3. The plate 6 consists of a elastic material that can apply an elastic force to the tube 5. Preferably the plate consists of a transparent material that allows visual inspection of the material in the "Eppendorf" tubes when these are inserted in the apertures 3.

To avoid that the force from the plate 6 shall be dependant of the number of tubes inserted i the device, the plate 6 is supplied with a number of slots 8, so that the tubes will be affected of segments that are independent of each other and defined between to adjacent slots 8.

In use the "Eppendorf" tubes containing a suspension of small balls, for instance the balls ore particles known as "Ugelstad's" balls, that for the present aim has been made super paramagnetic to be able to move in a magnetic field, but are separated from each other when the magnetic field cease to exist.

Dependant of the purpose, the balls are also coated with a material that has affinity to the macromolecules, proteins etc. that is intended to be separated from the liquid in which the particles are suspended. When a tube is inserted in an aperture 3, the particles will be affected by the magnet 4 and collect along the inner wall of the tube adjacent the magnet 4.

In the preferred embodiment the magnet 4 is a strong

permanent magnet since this makes the separation device simple to handle and simple to produce, but for certain purposes it can also be used electro-magnets. This can be advantageously i certain cases where it is wanted that the particles or balls are present in the separation device, so that the balls can float freely and the surface active coating can be i contact with the solution for a desired period of time. The electromagnets can for instance be activated simultaneously or in sequens according to a previous determined sequens.

Due to the fixation of the tube by the plate 6, the separation device with the inserted tubes can be shaken carefully, be turned so that possible particles fixed to the liquid surface, bubbles and so on can be brought into the suspension and thereafter move in the direction of the magnet 4 so that the most of or all the particulate material will be collected adjacent the inner wall of the tube adjacent the magnet. The supernatant liquid can be decanted, sucked up by means of a pipette or removed otherwise if this is wanted.

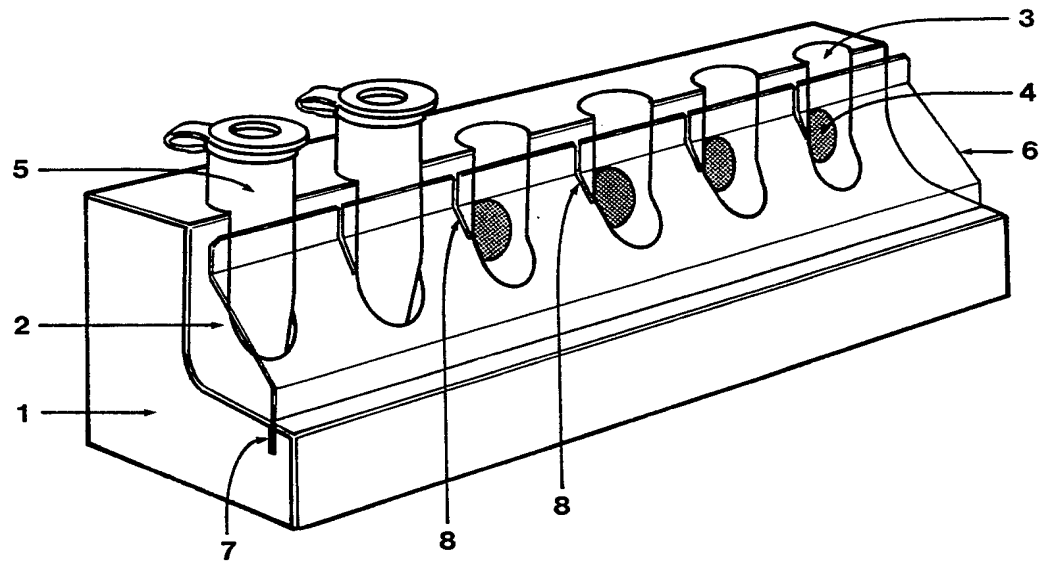
Even if the temporary preferred embodiment is designed as shown in the drawing, the separation device can of course have a design to receive a much larger number of tubes or be designed in such a way that other types of tubes can be accommodated in a larger model of the separation device than shown in the drawing.

The separation device need not be designed as rectilinear, but the tubes can for instance be arranged circumferentially in a carousel if this is preferred.

C l a i m s

1. Separation device for separating magnetizable particles provided with a coating for selective affinity for the compound or compounds to be removed form a liquid in which the particles are suspended, consisting of a rack (1) for tubes (5), preferably "Eppendorf" tubes, which rack is provided with at least one magnet (4) provided to affect the magnetizable particles when a tube is inserted in the rack, characterized in that the rack for receiving a number of tubes (5) is provided with a number of apertures (3), which tubes (5) intersects the magnets (4) fields.
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2. Separation device according to claim 1, characterized in that a resting-plate (6), preferably a transparent elastic material is provided to push a tube (5) against the wall of the aperture (3) towards the direction of a magnet (4).
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3. Separation device according to claim 2, characterized in that the plate (6) is provided with a number of slots (8).
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4. Separation device according to the previous claims, characterized in that the magnet (4) is a permanent magnet.
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5. Separation device according to claim 1 - 4, characterized in that the magnet (4) is a electromagnet.

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INTERNATIONAL SEARCH REPORT

International Application No PCT/NO 90/00098

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶ According to International Patent Classification (IPC) or to both National Classification and IPC IPC5: B 03 C 1/02, 1/28, B 01 L 9/06 // G 01 N 33/53																	
II. FIELDS SEARCHED <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black;">Minimum Documentation Searched⁷</div> <table style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 25%; border-bottom: 1px solid black;">Classification System</th> <th style="border-bottom: 1px solid black;">Classification Symbols</th> </tr> <tr> <td style="padding: 5px; vertical-align: top;">IPC5</td> <td style="padding: 5px; vertical-align: top;">B 03 C; B 01 L; G 01 N</td> </tr> </table> <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black;">Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in Fields Searched⁸</div> <p style="padding: 5px;">SE,DK,FI,NO classes as above</p>			Classification System	Classification Symbols	IPC5	B 03 C; B 01 L; G 01 N											
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III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹ <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 10%; padding: 5px;">Category *</th> <th style="width: 70%; padding: 5px;">Citation of Document,¹¹ with indication, where appropriate, of the relevant passages¹²</th> <th style="width: 20%; padding: 5px;">Relevant to Claim No.¹³</th> </tr> </thead> <tbody> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="padding: 5px;">DE, A1, 3102029 (EUROPÄISCHES LABORATORIUM FÜR MOLEKULARBIOLOGIE (EMBL)) 26 August 1982, see figures and claims --</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-5</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="padding: 5px;">EP, A2, 0136126 (CORNING GLASS WORKS) 3 April 1985, see figures and claims --</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-5</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="padding: 5px;">US, A, 4297337 (GERALD R. MANSFIELD ET AL) 27 October 1981, see column 8, line 63 - column 9, line 59 --</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1,4,5</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">P,X</td> <td style="padding: 5px;">US, A, 4895650 (ROBERT WANG) 23 January 1990, see column 3, line 59 - line 62; column 4, line 41 - line 44 figures and claims --</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-5</td> </tr> </tbody> </table>			Category *	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³	X	DE, A1, 3102029 (EUROPÄISCHES LABORATORIUM FÜR MOLEKULARBIOLOGIE (EMBL)) 26 August 1982, see figures and claims --	1-5	X	EP, A2, 0136126 (CORNING GLASS WORKS) 3 April 1985, see figures and claims --	1-5	X	US, A, 4297337 (GERALD R. MANSFIELD ET AL) 27 October 1981, see column 8, line 63 - column 9, line 59 --	1,4,5	P,X	US, A, 4895650 (ROBERT WANG) 23 January 1990, see column 3, line 59 - line 62; column 4, line 41 - line 44 figures and claims --	1-5
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<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>* Special categories of cited documents:¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p> </div> </div>																	
IV. CERTIFICATION <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; padding: 5px; vertical-align: top;"> Date of the Actual Completion of the International Search 29th August 1990 </td> <td style="width: 50%; padding: 5px; vertical-align: top;"> Date of Mailing of this International Search Report 1990 -09- 03 </td> </tr> <tr> <td style="padding: 5px; vertical-align: top;"> International Searching Authority SWEDISH PATENT OFFICE </td> <td style="padding: 5px; vertical-align: top;"> Signature of Authorized Officer Ulf Nyström </td> </tr> </table>			Date of the Actual Completion of the International Search 29th August 1990	Date of Mailing of this International Search Report 1990 -09- 03	International Searching Authority SWEDISH PATENT OFFICE	Signature of Authorized Officer Ulf Nyström											
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III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	US, A, 4438068 (GORDON C. FORREST) 20 March 1984, see the whole document -- -----	1

ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.PCT/NO 90/00098

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the Swedish Patent Office EDP file on 90-08-02
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE-A1- 3102029	82-08-26	NONE	
EP-A2- 0136126	85-04-03	CA-A- 1220168 JP-A- 60067858	87-04-07 85-04-18
US-A- 4297337	81-10-27	AU-B- 536077 AU-D- 5723480 DE-A- 3014036 FR-A-B- 2454098 GB-A-B- 2048470 JP-B- 1045579 JP-A- 55141670	84-04-19 80-10-16 80-10-23 80-11-07 80-12-10 89-10-04 80-11-05
US-A- 4895650	90-01-23	NONE	
US-A- 4438068	84-03-20	CA-A- 1152559 EP-A-B- 0030086	83-08-23 81-06-10